



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Art Unit : 1624
Examiner : Brenda Coleman
Applicant(s) : EJ Jacobsen, SK Hendges
Serial Number : 10/022,471
Filed : October 30, 2001
For : 1,2,3,4,5,6-Hexahydroazepino[4,5-B]Indoles Containing Arylsulfones At The 9-Position

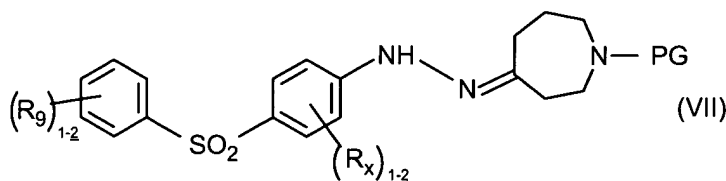
Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE UNDER 37 CFR § 1.111

Sir:

Examiner has made a 35 U.S.C. § 112 rejection regarding the pending claims 24 and 25, because there can be "1-" substituents of R_9 and R_x : " $(R_9)_1$ -" and " $(R_x)_1$ -" . Applicant respectfully requests that the following amendments be made and provides support where needed for the requested amendments:

(1a) Formula VII should read as follows:



Support for 1-2 R_9 substituents is found on page 5, line 1, where it is stated: "There can be either one or two R_9 substituents and" Support for 1-2 R_x substituents is found on page 5, lines 6-7, where it is stated: "There can be either one or two R_x groups." This correction needs to occur in Claim 24, page 34, line 10.

This same correction affects other formulas. The same correction to allow 1-2 R_9 or R_x substituents occurs at the following locations:

page 1, line 27;

SEP 16 2003
TECH CENTER 1600/2003

#7
9/22/03
O. Style

page 24, Chart A;
page 25, Chart B; and
page 26, Char C.

(1b) Claim 24 has been amended to incorporate the appropriate definitions from canceled claim 1, incorporating the other corrections as discussed herein and referenced to canceled claim 1 as originally filed.

(1c) Claim 25 has been amended to incorporate the appropriate definitions from canceled claim 19.

Applicants request that the following corrections be allowed with referenced support:

(A) For R_X :

(i) R_{X-2} and R_{X-3} are stated “to be defined as above” on page 3, line 10 and page 28, line 21. This is an apparent typographical omission. R_{X-2} and R_{X-3} are substituents as follows: $-C(O)N(R_{X-2}R_{X-3})$. R_{3-2} and R_{3-3} as well as R_{N-2} and R_{N-3} and R_{9-2} and R_{9-3} are off the same core substituent and these R_{-2} and R_{-3} have identical definitions. Please amend R_{X-2} and R_{X-3} to be similarly defined: -H and C_1 - C_4 alkyl, and where R_{X-2} and R_{X-3} are taken with the attached nitrogen atom to form a ring selected from the group consisting of 1-pyrrolidinyl, 1-piperazinyl and 1-morpholinyl. This will also be corrected in the amended claim 24 (from canceled claim 1 on page 28, line 21).

(ii) R_{X-4} is stated to “be defined as above” on page 3, line 11 and page 28, line 22. This is an apparent typographical omission. R_{X-4} is found as a substituent as follows: $-NH-SO_2-R_{X-4}$. R_{3-4} as well as R_{N-4} and R_{9-4} are off the same core substituent and these R_{-4} have identical definitions. Please amend R_{X-4} to be similarly defined: -H and C_1 - C_4 alkyl. This will also be corrected in the amended claim 24 (from canceled claim 1 on page 28, line 22).

(B) For “C₀-C₄-φ”, Applicants inadvertently omitted “alkyl” between “C₀-C₄” and “-φ”. Support for having “alkyl” between “C₀-C₄” and “-φ” is found on page 9, lines 4-10, where subscripted carbon atoms is discussed. Please amend “C₀-C₄-φ” to read “C₀-C₄alkyl-φ” at the following locations:

page 1, line 31;

page 2, line 19;

page 3, line 23;

page 27, lines 7 and 26 (will be corrected in amended claim 24); and

page 29, line 1 (will be corrected in amended claim 24).

(C) For many substituents, (I) should read (i). Please correct this typographical error at the following locations:

page 2, line 14 and line 33;

page 4, line 4

page 29, line 15 (will be corrected in amended claim 24).

(D) Please delete “aa” on page 6, line 11 of the specification. This is a typographical inclusion.

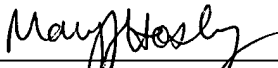
Amendments are attached.

CONCLUSION

Accordingly, it is believed that claims 24-25 are now in condition for allowance, early notice of which would be appreciated.

If any outstanding issues remain, Examiner is invited to telephone the undersigned to discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees or credit overpayment to Deposit Account No. 21-0718.

Respectfully submitted,



Mary Hosley, Attorney
Registration No. 48,324

Date: 9 September 2003

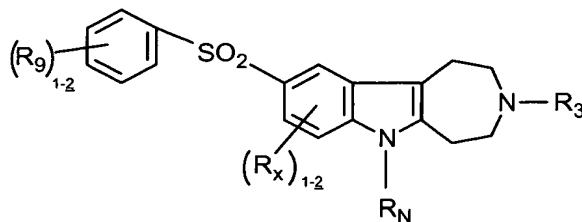
Pharmacia & Upjohn Company
Global Intellectual Property
301 Henrietta Street
Kalamazoo, Michigan 49001

Telephone No. (269) 833-0975 or (269) 833-9500
Telefax No. (269) 833-8897 or (269) 833-2316



Specification

Disclosed is a 9-arylsulfone of the formula (XII)

where R₃ is:

- 5 (1) -H,
 (2) C₁-C₄ alkyl,
 (3) C₀-C₄ alkyl-φ where the -φ substituent is optionally substituted with 1 or 2
 (a) -F, -Cl, -Br, -I,
 (b) -O-R₃₋₁ where R₃₋₁ is:
 10 -H,
 C₁-C₄ alkyl,
 -φ,
 (c) -CF₃,
 (d) -CO-NR₃₋₂R₃₋₃ where R₃₋₂ and R₃₋₃ are -H and C₁-C₄ alkyl, and
 15 where R₃₋₂ and R₃₋₃ are taken with the attached nitrogen atom to form a ring selected
 from the group consisting of 1-pyrrolidinyl, 1-piperazinyl and 1-morpholinyl,
 (e) -NH-SO₂-R₃₋₄ where R₃₋₄ is -H and C₁-C₄ alkyl,
 (f) -NR₃₋₂R₃₋₃ where R₃₋₂ and R₃₋₃ are as defined above,
 (g) -NR₃₋₄-CO-R₃₋₄ where R₃₋₄ is as defined above,
 20 (h) -SO₂-NR₃₋₂R₃₋₃ where R₃₋₂ and R₃₋₃ are as defined above,
 (i) -C≡N,
 (j) -NO₂,

where R_N is:

- 25 (1) -H,
 (2) C₁-C₄ alkyl,
 (3) C₀-C₄ alkyl-φ where the -φ substituent is optionally substituted with 1 or 2
 (a) -F, -Cl, -Br, -I,
 (b) -O-R_{N-1} where R_{N-1} is
 -H,

C₁-C₄ alkyl,

-φ,

(c) -CF₃,

(d) -CO-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are -H and C₁-C₄ alkyl, and

5 where R₃₋₂ and R₃₋₃ are taken with the attached nitrogen atom to form a ring selected from the group consisting of 1-pyrrolidinyl, 1-piperazinyl and 1-morpholinyl,

(e) -NH-SO₂-R_{N-4} where R_{N-4} is -H and C₁-C₄ alkyl,

(f) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined above,

(g) -NR_{N-4}-CO-R_{N-4} where R_{N-4} is as defined above,

10 (h) -SO₂-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined above,

(i) -C≡N,

(j) -NO₂,

where R_X is:

(1) -H

15 (2) -F, -Cl, -Br, -I,

(3) -O-R_{X-1} where R_{X-1} is:

-H,

C₁-C₄ alkyl,

-φ,

20 (4) -CF₃,

(5) -CO-NR_{X-2}R_{X-3} where R_{X-2} and R_{X-3} are ~~as defined above~~ -H and C₁-C₄

alkyl, and where R_{X-2} and R_{X-3} are taken with the attached nitrogen atom to form a ring selected from the group consisting of 1-pyrrolidinyl, 1-piperazinyl and 1-morpholinyl,

(6) -NH-SO₂-R_{X-4} where R_{X-4} is ~~as defined above~~ -H and C₁-C₄ alkyl,

25 (7) -NR_{X-2}R_{X-3} where R_{X-2} and R_{X-3} are as defined above,

(8) -NR_{X-4}-CO-R_{X-4} where R_{X-4} is as defined above,

(9) -SO₂-NR_{X-2}R_{X-3} where R_{X-2} and R_{X-3} are as defined above,

(10) -C≡N,

(11) -NO₂;

30 where R₉ is:

(1) -H,

(2) -F, -Cl,

(3) C₁-C₄ alkyl,

(4) C₁-C₃ alkoxy,

(5) -CF₃,

(6) C₀-C₄ alkyl-φ where the -φ substituent is optionally substituted with 1 or 2

(a) -F, -Cl, -Br, -I,

5 (b) -O-R₉₋₁ where R₉₋₁ is:

-H,

C₁-C₄ alkyl,

-φ,

(c) -CF₃,

10 (d) -CO-NR₉₋₂R₉₋₃ where R₉₋₂ and R₉₋₃ are -H and C₁-C₄ alkyl, and

where R₉₋₂ and R₉₋₃ are taken with the attached nitrogen atom to form a ring selected from the group consisting of 1-pyrrolidiny, 1-piperaziny and 1-morpholinyl,

(e) -NH-SO₂-R₉₋₄ where R₉₋₄ is -H and C₁-C₄ alkyl,

(f) -NR₉₋₂R₉₋₃ where R₉₋₂ and R₉₋₃ are as defined above,

15 (g) -NR₉₋₄-CO-R₉₋₄ where R₉₋₄ is as defined above,

(h) -SO₂-NR₉₋₂R₉₋₃ where R₉₋₂ and R₉₋₃ are as defined above,

(i) -C≡N,

(j) -NO₂

(7) -OR₉₋₁ where R₉₋₁ is as defined above,

20 (8) -CO-NR₉₋₂R₉₋₃ where R₉₋₂ and R₉₋₃ are as defined above,

(9) -NR₉₋₂R₉₋₃ where R₉₋₂ and R₉₋₃ are as defined above,

(10) -NH-SO₂-R₉₋₄ where R₉₋₄ is as defined above,

(11) -NH-CO₂-R₉₋₂ where R₉₋₂ is as defined above,

and pharmaceutically acceptable salts thereof.

25

The 9-arylsulfones (XI) are amines, and as such form acid addition salts when reacted with acids of sufficient strength. Pharmaceutically acceptable salts include salts of both inorganic and organic acids. The pharmaceutically acceptable salts are preferred over the corresponding free amines since they produce compounds which
5 are more water soluble and more crystalline. The preferred pharmaceutically acceptable salts include salts of the following acids methanesulfonic, hydrochloric, hydrobromic, sulfuric, phosphoric, nitric, benzoic, citric, tartaric, fumaric, maleic, $\text{CH}_3-(\text{CH}_2)_n\text{-COOH}$ where n is 0 thru 4, $\text{HOOC}-(\text{CH}_2)_N\text{-COOH}$ where n is as defined above. aa

10

Chart A

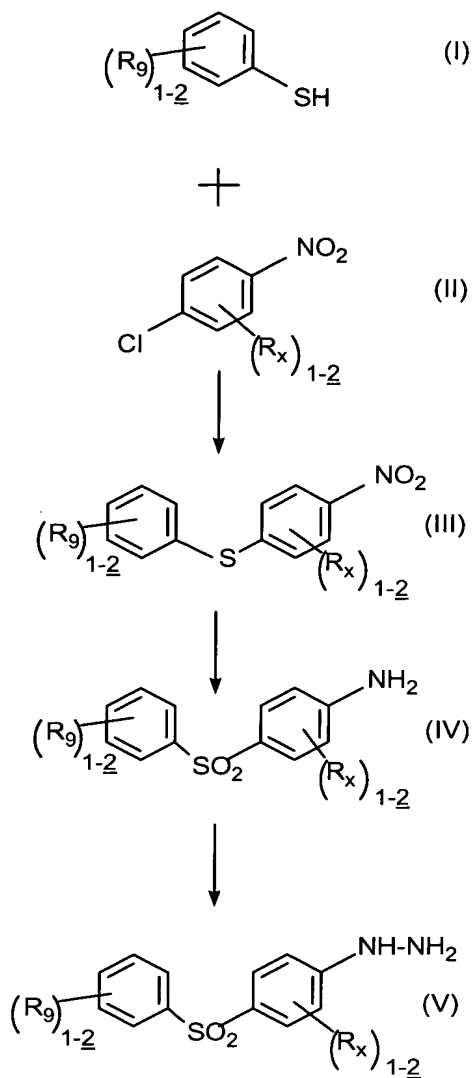


Chart B

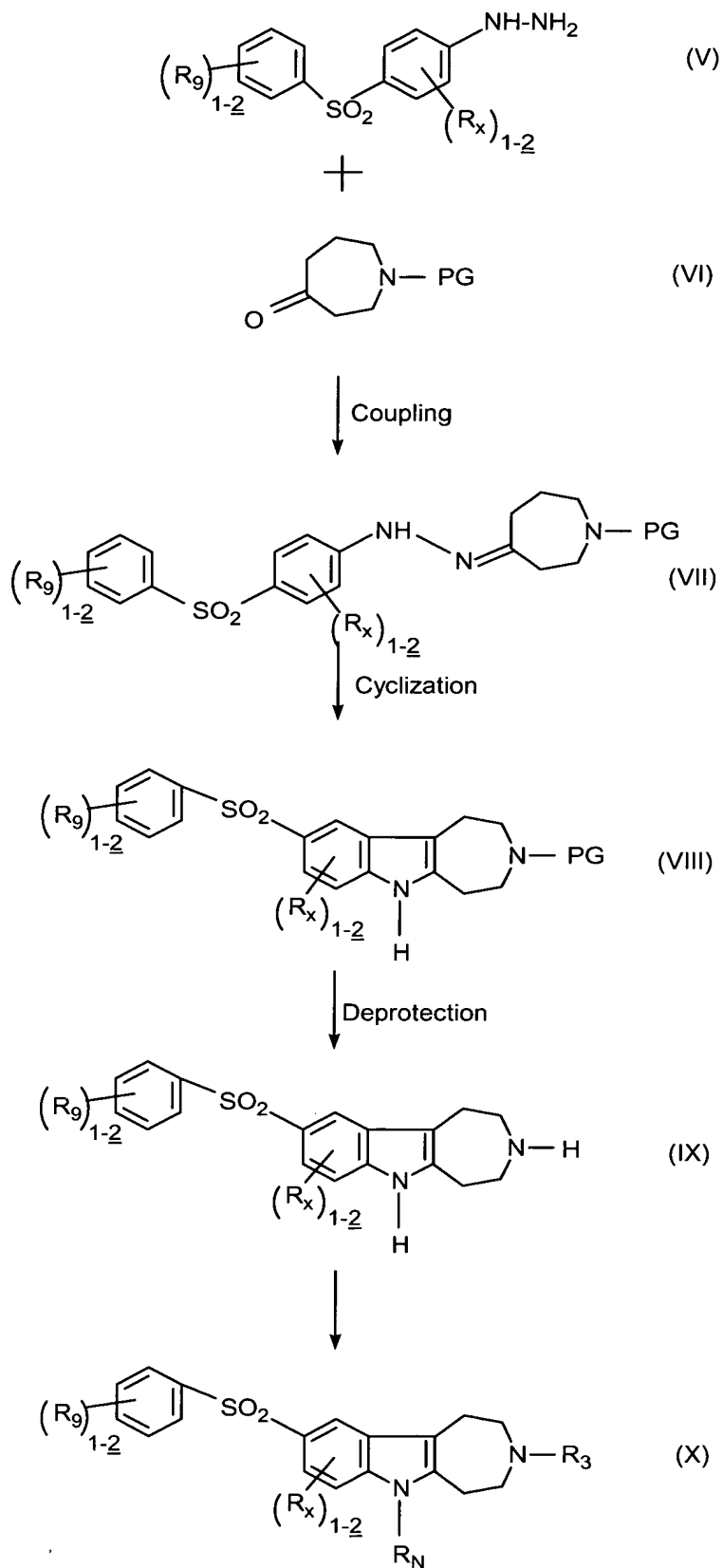
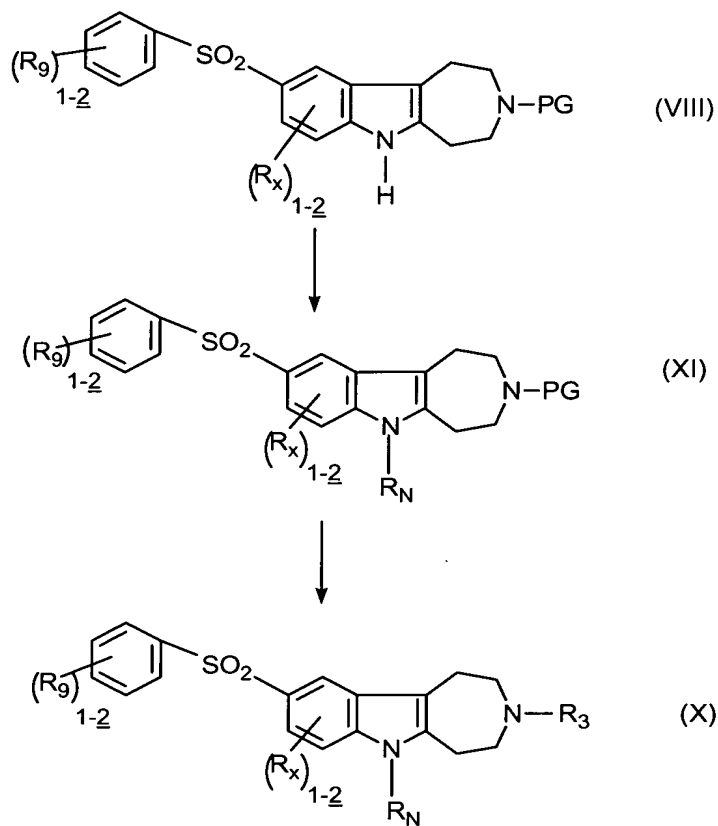
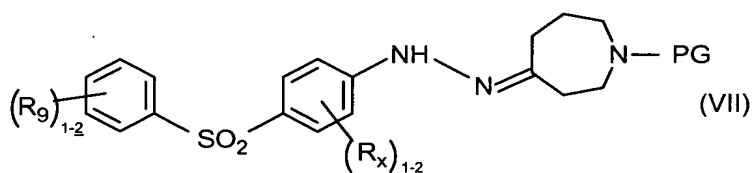


Chart C



Claims

- Claim 1. Previously canceled.
- Claim 2. Previously canceled.
- Claim 3. Previously canceled.
- 5 Claim 4. Previously canceled.
- Claim 5. Previously canceled.
- Claim 6. Previously canceled.
- Claim 7. Previously canceled.
- Claim 8. Previously canceled.
- 10 Claim 9. Previously canceled.
- Claim 10. Previously canceled.
- Claim 11. Previously canceled.
- Claim 12. Previously canceled.
- Claim 13. Previously canceled.
- 15 Claim 14. Previously canceled.
- Claim 15. Previously canceled.
- Claim 16. Previously canceled.
- Claim 17. Previously canceled.
- Claim 18. Previously canceled.
- 20 Claim 19. Previously canceled.
- Claim 20. Previously canceled.
- Claim 21. Previously canceled.
- Claim 22. Previously canceled.
- Claim 23. Previously canceled.
- 25 Claim 24 (Currently amended) A compound of formula (VII)



where PG is selected from the group consisting of ϕ -CH₂-, ϕ -CO-, ϕ -CH₂-CO₂- and -CO-O-C(CH₃)₃, ~~where R₉ and R_x are as defined in claim 1.~~

where R_x is:

- 30 (1) -H
- (2) -F, -Cl, -Br, -I,

- (3) -O-R_{X-1} where R_{X-1} is:
-H,
C₁-C₄ alkyl,
-φ,
- 5 (4) -CF₃,
(5) -CO-NR_{X-2}R_{X-3} where R_{X-2} and R_{X-3} are -H and C₁-C₄ alkyl, and where R_{X-2}
and R_{X-3} are taken with the attached nitrogen atom to form a ring selected from the
group consisting of 1-pyrrolidinyl, 1-piperazinyl and 1-morpholinyl,
- (6) -NH-SO₂-R_{X-4} where R_{X-4} is -H and C₁-C₄ alkyl,
- 10 (7) -NR_{X-2}R_{X-3} where R_{X-2} and R_{X-3} are as defined above,
(8) -NR_{X-4}-CO-R_{X-4} where R_{X-4} is as defined above,
(9) -SO₂-NR_{X-2}R_{X-3} where R_{X-2} and R_{X-3} are as defined above,
(10) -C≡N,
(11) -NO₂; and
- 15 where R₉ is:
(1) -H,
(2) -F, -Cl,
(3) C₁-C₄ alkyl,
(4) C₁-C₃ alkoxy,
- 20 (5) -CF₃,
(6) C₀-C₄ alkyl-φ where the -φ substituent is optionally substituted with 1 or 2
(a) -F, -Cl, -Br, -I,
(b) -O-R₉₋₁ where R₉₋₁ is:
-H,
- 25 C₁-C₄ alkyl,
-φ,
(c) -CF₃,
(d) -CO-NR₉₋₂R₉₋₃ where R₉₋₂ and R₉₋₃ are -H and C₁-C₄ alkyl, and
where R₉₋₂ and R₉₋₃ are taken with the attached nitrogen atom to form a ring selected
from the group consisting of 1-pyrrolidinyl, 1-piperazinyl and 1-morpholinyl,
- 30 (e) -NH-SO₂-R₉₋₄ where R₉₋₄ is -H and C₁-C₄ alkyl,
(f) -NR₉₋₂R₉₋₃ where R₉₋₂ and R₉₋₃ are as defined above,
(g) -NR₉₋₄-CO-R₉₋₄ where R₉₋₄ is as defined above,

- (h) -SO₂-NR_{9.2}R_{9.3} where R_{9.2} and R_{9.3} are as defined above,
- (i) -C≡N,
- (j) -NO₂
- (7) -OR_{9.1} where R_{9.1} is as defined above,
- 5 (8) -CO-NR_{9.2}R_{9.3} where R_{9.2} and R_{9.3} are as defined above,
- (9) -NR_{9.2}R_{9.3} where R_{9.2} and R_{9.3} are as defined above,
- (10) -NH-SO₂-R_{9.4} where R_{9.4} is as defined above,
- (11) -NH-CO₂-R_{9.2} where R_{9.2} is as defined above.
- 10 Claim 25 (Currently amended) A compound according to claim 24 where PG is ϕ -CH₂- or ϕ -CO- and ~~where R₉ and R_x are as defined in claim 19.~~ where R₉ is selected from the group consisting of -H, -F, -Cl, C₁-C₃ alkyl, C₁-C₃ alkoxy and -CF₃ and where R_x is selected from the group consisting of -H, -F and -Cl.
- 15 Claim 26. Previously canceled.
- Claim 27. Previously canceled.
- Claim 28. Previously canceled.
- Claim 29. Previously canceled.
- Claim 31. Previously canceled.
- 20 Claim 32. Previously canceled.
- Claim 33. Previously canceled.
- Claim 34. Previously canceled.
- Claim 35. Previously canceled.
- Claim 36. Previously canceled.
- 25 Claim 37. Previously canceled.